junctional epidermolysis bullosa

Junctional epidermolysis bullosa (JEB) is one of the major forms of epidermolysis bullosa, a group of genetic conditions that cause the skin to be very fragile and to blister easily. Blisters and skin erosions form in response to minor injury or friction, such as rubbing or scratching. Researchers classify junctional epidermolysis bullosa into two main types: Herlitz JEB and non-Herlitz JEB. Although the types differ in severity, their features overlap significantly, and they can be caused by mutations in the same genes.

Herlitz JEB is the more severe form of the condition. From birth or early infancy, affected individuals have blistering over large regions of the body. Blistering also affects the mucous membranes, such as the moist lining of the mouth and digestive tract, which can make it difficult to eat and digest food. As a result, many affected children have chronic malnutrition and slow growth. The extensive blistering leads to scarring and the formation of red, bumpy patches called granulation tissue. Granulation tissue bleeds easily and profusely, making affected infants susceptible to serious infections and loss of necessary proteins, minerals, and fluids. Additionally, a buildup of granulation tissue in the airway can lead to a weak, hoarse cry and difficulty breathing.

Other complications of Herlitz JEB can include fusion of the fingers and toes, abnormalities of the fingernails and toenails, joint deformities (contractures) that restrict movement, and hair loss (alopecia). Because the signs and symptoms of Herlitz JEB are so severe, infants with this condition usually do not survive beyond the first year of life.

The milder form of junctional epidermolysis bullosa is called non-Herlitz JEB. The blistering associated with non-Herlitz JEB may be limited to the hands, feet, knees, and elbows, and it often improves after the newborn period. Other characteristic features of this condition include alopecia, malformed fingernails and toenails, and irregular tooth enamel. Most affected individuals do not have extensive scarring or granulation tissue formation, so breathing difficulties and other severe complications are rare. Non-Herlitz JEB is typically associated with a normal lifespan.

Frequency

Both types of junctional epidermolysis bullosa are rare, affecting fewer than 1 per million people in the United States.

Genetic Changes

Junctional epidermolysis bullosa results from mutations in the *LAMA3*, *LAMB3*, *LAMC2*, and *COL17A1* genes. Mutations in each of these genes can cause Herlitz JEB or non-

Herlitz JEB. *LAMB3* gene mutations are the most common, causing about 70 percent of all cases of junctional epidermolysis bullosa.

The *LAMA3*, *LAMB3*, and *LAMC2* genes each provide instructions for making one part (subunit) of a protein called laminin 332. This protein plays an important role in strengthening and stabilizing the skin by helping to attach the top layer of skin (the epidermis) to underlying layers. Mutations in any of the three laminin 332 genes lead to the production of a defective or nonfunctional version of this protein. Without functional laminin 332, cells in the epidermis are fragile and easily damaged. Friction or other minor trauma can cause the skin layers to separate, leading to the formation of blisters.

The *COL17A1* gene provides instructions for making a protein that is used to assemble type XVII collagen. Collagens are molecules that give structure and strength to connective tissues, such as skin, tendons, and ligaments, throughout the body. Type XVII collagen helps attach the epidermis to underlying layers of skin, making the skin strong and flexible. Mutations in the *COL17A1* gene prevent the normal formation of collagen XVII. As a result, the skin is less resistant to friction and minor trauma and blisters easily. Most *COL17A1* gene mutations cause non-Herlitz JEB, although a few individuals with mutations in this gene have had the more severe Herlitz JEB.

Inheritance Pattern

Both types of junctional epidermolysis bullosa are inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Epidermolysis Bullosa, Junctional
- JEB

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Adult junctional epidermolysis bullosa
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268374/
- Genetic Testing Registry: Epidermolysis bullosa, junctional
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0079301/
- Genetic Testing Registry: Junctional epidermolysis bullosa gravis of Herlitz
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0079683/

Other Diagnosis and Management Resources

- Epidermolysis Bullosa Center, Cincinnati Children's Hospital Medical Center
  https://www.cincinnatichildrens.org/service/e/epidermolysis-bullosa
- GeneReview: Junctional Epidermolysis Bullosa
  https://www.ncbi.nlm.nih.gov/books/NBK1125
- MedlinePlus Encyclopedia: Epidermolysis Bullosa
  https://medlineplus.gov/ency/article/001457.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Epidermolysis Bullosa
  https://medlineplus.gov/ency/article/001457.htm
- Health Topic: Skin Conditions
  https://medlineplus.gov/skinconditions.html

Genetic and Rare Diseases Information Center

- Epidermolysis bullosa
  https://rarediseases.info.nih.gov/diseases/6359/epidermolysis-bullosa
- Junctional epidermolysis bullosa
  https://rarediseases.info.nih.gov/diseases/2152/junctional-epidermolysis-bullosa

Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases
  https://www.niams.nih.gov/Health_Info/Epidermolysis_Bullosa/epidermolysis_bullosa_ff.asp

Educational Resources

- Disease InfoSearch: Adult junctional epidermolysis bullosa
  http://www.diseaseinfosearch.org/Adult+junctional+epidermolysis+bullosa/7640
- Disease InfoSearch: Epidermolysis Bullosa, Junctional
  http://www.diseaseinfosearch.org/Epidermolysis+Bullosa%2C+Junctional/2588
- MalaCards: junctional epidermolysis bullosa
  http://www.malacards.org/card/junctional_epidermolysis_bullosa
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Junctional%20Epidermolysis%20Bullosa&type=profile
- Orphanet: Junctional epidermolysis bullosa
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=305

Patient Support and Advocacy Resources

- DebRA UK
  https://www.debra.org.uk/
- Dystrophic Epidermolysis Bullosa Research Association of America (DebRA)
  http://www.debra.org/
- Epidermolysis Bullosa Medical Research Foundation
  http://www.ebkids.org/
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/epidermolysis-bullosa/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/epidermo.html

GeneReviews

- Junctional Epidermolysis Bullosa
  https://www.ncbi.nlm.nih.gov/books/NBK1125

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Epidermolysis+Bullosa%22+OR+%22junctional+epidermolysis+bullosa%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Epidermolysis+Bullosa,+Junctional%5BMAJR%5D%29+AND+%28%28epidermolysis+bullosa%5BTIAB%5D%29+AND+%28junctional%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- EPIDERMOLYSIS BULLOSA, JUNCTIONAL, HERLITZ TYPE
  http://omim.org/entry/226700
- EPIDERMOLYSIS BULLOSA, JUNCTIONAL, NON-HERLITZ TYPE
  http://omim.org/entry/226650

Sources for This Summary

- Castori M, Floriddia G, De Luca N, Pascucci M, Ghirri P, Boccaletti V, El Hachem M, Zambruno G, Castiglia D. Herlitz junctional epidermolysis bullosa: laminin-5 mutational profile and carrier frequency in the Italian population. Br J Dermatol. 2008 Jan;158(1):38-44. Epub 2007 Oct 4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17916201
- Fine JD, Eady RA, Bauer EA, Bauer JW, Bruckner-Tuderman L, Heagerty A, Hintner H, Hovnanian A, Jonkman MF, Leigh I, McGrath JA, Mellerio JE, Murrell DF, Shimizu H, Uitto J, Vahlquist A, Woodley D, Zambruno G. The classification of inherited epidermolysis bullosa (EB): Report of the Third International Consensus Meeting on Diagnosis and Classification of EB. J Am Acad Dermatol. 2008 Jun;58(6):931-50. doi: 10.1016/j.jaad.2008.02.004. Epub 2008 Apr 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18374450
- GeneReview: Junctional Epidermolysis Bullosa
  https://www.ncbi.nlm.nih.gov/books/NBK1125
- Mühle C, Jiang QJ, Charlesworth A, Bruckner-Tuderman L, Meneguzzi G, Schneider H. Novel and recurrent mutations in the laminin-5 genes causing lethal junctional epidermolysis bullosa: molecular basis and clinical course of Herlitz disease. Hum Genet. 2005 Jan;116(1-2):33-42. Epub 2004 Nov 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15538630
- Nakano A, Lestringant GG, Paperna T, Bergman R, Gershoni R, Frossard P, Kanaan M, Meneguzzi G, Richard G, Pfendner E, Uitto J, Pulkkinen L, Sprecher E. Junctional epidermolysis bullosa in the Middle East: clinical and genetic studies in a series of consanguineous families. J Am Acad Dermatol. 2002 Apr;46(4):510-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11907499
- Pfendner EG, Bruckner A, Conget P, Mellerio J, Palisson F, Lucky AW. Basic science of epidermolysis bullosa and diagnostic and molecular characterization: Proceedings of the IInd International Symposium on Epidermolysis Bullosa, Santiago, Chile, 2005. Int J Dermatol. 2007 Aug;46(8):781-94.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17651158

- Pulkkinen L, Uitto J. Mutation analysis and molecular genetics of epidermolysis bullosa. Matrix Biol. 1999 Feb;18(1):29-42. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10367729
- Varki R, Sadowski S, Pfendner E, Uitto J. Epidermolysis bullosa. I. Molecular genetics of the junctional and hemidesmosomal variants. J Med Genet. 2006 Aug;43(8):641-52. Epub 2006 Feb 10.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16473856
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2564586/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/junctional-epidermolysis-bullosa

Reviewed: September 2009
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services